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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,641	07/27/2001	Marc Pignot	11413-003001	3092

7590 03/24/2004

Fish & Richardson
4350 La Jolla Village Drive Suite 500
San Diego, CA 92122

EXAMINER	
LEWIS, PATRICK T	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 03/24/2004

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,641	PIGNOT ET AL.	
	Examin r	Art Unit	
	Patrick T. Lewis	1623	

-- The MAILING DATE of this communication appears on the c ver sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19 and 21-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19 and 21-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's Response dated August 11, 2003

1. In the Response filed August 11, 2003, claims 1-11, 14-19, and 21-30 were amended; claim 20 was canceled; and claims 31-43 were added. Applicant presented a declaration under 37 C.F.R. 1.132 and arguments directed to the rejection of claims 1-15 and 27 under 35 U.S.C. 112, first paragraph; the rejection of claims 9, 10, and 13 under 35 U.S.C. 112, first paragraph; and the rejection of claims 1-15 and 21-27 under 35 U.S.C. 112, second paragraph.

2. Claims 1-19 and 21-43 are pending. An action on the merits of claims 1-19 and 21-43 is contained herein below.

3. The rejection of claims 1-15 and 27 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record as set forth in the Office Action dated April 7, 2003.

4. The rejection of claims 9, 10, and 13 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record as set forth in the Office Action dated April 7, 2003.

5. The rejection of claims 1-15 and 21-27 under 35 U.S.C. 112, second paragraph is maintained for the reasons of record as set forth in the Office Action dated April 7, 2003.

Objections/Rejections of Record Set Forth in Office Action dated April 7, 2003

6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

7. Claims 1-15 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds of formulae 2 and 9 on pages 12 and 16 of the specification, respectively, i.e. wherein X is N, Y is N, and n is 1-4, does not reasonably provide enablement for the broad genus of compounds of formula (I), and in particular for compounds wherein X is not N, Y is not N, R^2 is not H and n is up to 5000. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The declaration under 37 CFR 1.132 filed August 11, 2003 is insufficient to overcome the rejection of claims 1-15 and 27 based upon insufficiency of disclosure under 35 U.S.C. 112, first paragraph, as set forth in the last Office action because: the declaration fails to set forth sufficient evidence or convincing facts.

Declarations attempting to show that applicant's disclosure is enabling should meet the following criteria:

1. the affidavit/declaration must present a showing of enablement which is commensurate with the claims (in other words the number of examples must be sufficient to show enablement for the entire scope of the claimed subject matter or at least the objected to subject matter);
2. the evidence presented must not be directed to information that should have been in the specification; and

3. the affidavit/declaration must establish that the hypothetetical person of ordinary skill in the art would have been enabled to practice the claimed subject matter without undue experimentation.

Applicant further argues that the quantity of experimentation necessary is not "undue", citing *Hybritech, Inc. v. Monoclonal Antibodies, Inc.* (Hybritech) as basis. Hybritech is noted; however, it is not seen to be germane. Conclusions of enablement must be made based on the facts relating to the specifics of the individual invention/application rather than liberal interpretation of any one individual court decision. The facts in the Hybritech decision and the instant rejection are not analogous. Firstly, it should be noted that the instant rejection is a scope of enablement rejection rather than lack of enablement. It should also be noted that the antibodies of the Hybritech decision are produced by a distinct, well-known process [hybridoma] while in the instant case, one of ordinary skill in the art would be required to design a synthetic scheme, determine appropriate reaction conditions, and screen a large number of alternative protocols to determine if the synthesized species would act as a co-factor for a SAM-dependent methyltransferase.

8. Claims 9-10 and 13 are further rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the complexes with DNA methyltransferases, such as M•Taq1, M•Hha1, does not reasonably provide enablement for the broad genus of methyltransferases, such as polypeptide, protein, enzyme or small molecule methyltransferases, as instantly claimed. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The declaration under 37 CFR 1.132 filed August 11, 2003 is insufficient to overcome the rejection of claims 1-15 and 27 based upon insufficiency of disclosure under 35 U.S.C. 112, first paragraph, as set forth in the last Office action because: the declaration fails to set forth facts.

Declarations attempting to show that applicant's disclosure is enabling should meet the following criteria:

1. the affidavit/declaration must present a showing of enablement which is commensurate with the claims (in other words the number of examples must be sufficient to show enablement for the entire scope of the claimed subject matter or at least the objected to subject matter);
2. the evidence presented must not be directed to information that should have been in the specification; and
3. the affidavit/declaration must establish that the hypothetetical person of ordinary skill in the art would have been enabled to practice the claimed subject matter without undue experimentation.

Applicant's assertion that the required experimentation would be "routine" and not "undue" is noted but is not found persuasive. As set forth supra, the specification fails to teach one of ordinary skill in the art at the time of the invention how to make compounds of Formula (I) as broadly claimed. One of ordinary skill in the art would be required to design a synthetic scheme, determine appropriate reaction conditions, and

then screen a large number of alternative protocols to determine if the synthesized species would act as a co-factor for a specific SAM-dependent methyltransferase. The art at the time the invention was made fails to establish predictability with regard to how to make and use the complex of the aziridine derivatives with any methyltransferase as instantly claimed.

9. Claims 1-15 and 21-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's arguments with regard to the phrase "electron withdrawing group" have been found persuasive; however, the phrases "amino acids which may optionally be modified", "modified amino acids", "derivatives thereof", "aldehyde derivative", and "small molecule" still render claims in which they appear indefinite. Arguments that terms were known in the art at the time of the invention are not found persuasive. Applicant's amendments filed August 11, 2003 fail to obviate the rejections of record.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 16-19, 21-26, 28-41, and 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds of formulae 2 and 9 on pages 12 and 16 of the specification, respectively, i.e. wherein X is

N, Y is N, and n is 1-4, does not reasonably provide enablement for the broad genus of compound of formula (I), and in particular for compounds wherein X is not N, Y is not N, R^2 is not H and n is up to 5000. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

The factors include, but are not limited to:

1. The breadth of the claims,
2. The nature of the invention,
3. The state of the prior art,
4. The level of one of ordinary skill,
5. The level of predictability in the art,
6. The amount of direction provided by the inventor,
7. The existence of working examples, and
8. The quantity of experimentation needed to make and/or use the invention based on the content of the disclosure.

With regards to factors 1-5, it is noted that there is a great deal of unpredictability in the art. For example, there is no synthetic method that can be broadly applied to linking a group comprising one methylene chain as well as linking a group comprising more than 4 repeat units. Further, the three-dimensional structures of several methyltransferases in complex with the natural cofactor have indicated that the 8-

position of the adenine ring of the natural cofactor is at least partly assessable to solvent. However, in some methyltransferases, the 7-position of the adenine ring is more exposed to solvent. Therefore, the art fails to establish a pattern between derivatives in the 7 or 8 position and specificity for a broad class of methyltransferases. The art at the time of the invention was made fails to establish predictability with regard to how to make the aziridine derivatives as instantly claimed.

With regard to factors 6, 7, and 8, undue experimentation is required to determine how to make the compounds other than compounds of the formulae 2 and 9 on pages 12 and 16 of the specification respectively. There has not been provided adequate guidance in the written description for accomplishing such, as only two different aziridine analogs were synthesized, out of the limitless analogs encompassed with the broad genus. It is noted that Law requires that the disclosure of an application shall inform those skilled in the art how to make applicant's alleged discovery, now how to find out how to make it for themselves.

12. Claims 16-19 and 28-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The terms "modified amino acids", "derivatives thereof", "aldehyde derivative" and "small molecule" renders claims in which they appear indefinite. In the absence of specific modifications to the chemical core, distinct language to describe structural modifications, or names of the modified or "small" compounds, the identity of said compounds would be difficult to describe and the metes and bounds of the compounds

applicant regards as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claims.

Conclusion

13. Claims 1-19 and 21-43 are pending. Claims 1-19 and 21-43 are rejected. No claims are allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on M-F 10:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patrick T. Lewis, PhD
Examiner
Art Unit 1623

James O. Wilson
Supervisory Patent Examiner
Technology Center 1600

ptl
March 17, 2004